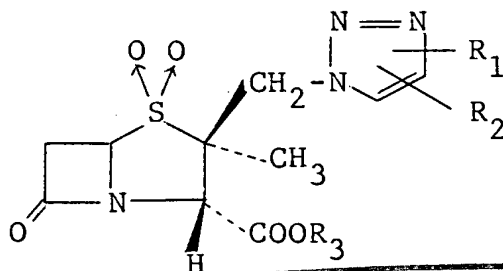


CM W. CLAIMS:

1. A penicillin derivative represented by the following formula

T590X



PS 5 wherein  $R_1$  is hydrogen or trialkylsilyl;  $R_2$  is hydrogen,  
 40 trialkylsilyl or  $\text{COOR}_2'$  wherein  $R_2'$  is hydrogen,  $\text{C}_{1-18}$   
 alkyl,  $\text{C}_{2-7}$  alkoxyethyl,  $\text{C}_{3-8}$  alkylcarbonyloxyethyl,  
 $\text{C}_{4-9}$  alkylcarbonyloxyethyl, ( $\text{C}_{5-7}$  cycloalkyl)carbonyloxy-  
 methyl,  $\text{C}_{9-14}$  benzylcarbonyloxyalkyl,  $\text{C}_{3-8}$  alkoxy-  
 10 carbonylmethyl,  $\text{C}_{4-9}$  alkoxy-carbonyloxyethyl, phthalidyl,  
 65 crotonolacton-4-yl,  $\gamma$ -butyrolacton-4-yl, halogenated  
 $\text{C}_{1-6}$  alkyl substituted with 1 to 3 halogen atoms,  $\text{C}_{1-6}$   
 alkoxy- or nitro-substituted or unsubstituted benzyl,  
 benzhydryl, tetrahydropyranyl, dimethylaminoethyl,  
 15 dimethylchlorosilyl, trichlorosilyl, (5-substituted  
 $\text{C}_{1-6}$  alkyl or phenyl or unsubstituted-2-oxo-1,3-dioxodene  
 4-yl)methyl,  $\text{C}_{8-13}$  benzoyloxyalkyl or group for forming  
 a pharmaceutically acceptable salt; and  $R_3$  has the same  
 40 meaning as above  $R_2'$ .

20 2. The penicillin derivative as defined in  
 claim 1 wherein  $R_3$  is  $\text{C}_{2-7}$  alkoxyethyl.

51

3. The penicillin derivative as defined in claim 1 wherein  $R_3$  is  $C_{3-8}$  alkylcarbonyloxymethyl,  $C_{4-9}$  alkylcarbonyloxyethyl, ( $C_{5-7}$  cycloalkyl)carbonyloxymethyl,  $C_{9-14}$  benzylcarbonyloxyalkyl or  $C_{8-13}$  benzoyloxyalkyl.

5            4. The penicillin derivative as defined in claim 1 wherein  $R_3$  is  $C_{3-8}$  alkoxycarbonylmethyl or  $C_{4-9}$  alkoxycarbonylethyl.

5. The penicillin derivative as defined in claim 1 wherein  $R_3$  is phthalidyl.

10           6. The penicillin derivative as defined in claim 1 wherein  $R_3$  is crotonolacton-4-yl and  
65  $\gamma$ -butyrolacton-4-yl.

7. The penicillin derivative as defined in claim 1 wherein  $R_3$  is (5-substituted  $C_{1-6}$  alkyl or  
15 phenyl or unsubstituted-2-oxo-1,3-dioxoden-4-yl)methyl.

8. The penicillin derivative as defined in claim 1 wherein  $R_3$  is a group for forming a pharmaceutically acceptable salt.

9. The penicillin derivative as defined in  
20 claim 1 wherein  $R_3$  is  $C_{1-6}$  alkyl or halogenated  $C_{1-6}$  alkyl substituted with 1 to 3 halogen atoms,  $C_{1-6}$  alkoxy- or nitro-substituted or unsubstituted benzyl, benzhydryl, tetrahydropyranyl, dimethylchlorosilyl and trichlorosilyl.

10. The penicillin derivative as defined in /

25  
Sub  
P  
ND  
claim 10

60

*B* *NK*  
*NP* claim 8 wherein the group for forming a pharmaceutically acceptable salt represented by  $R_3$  is alkali metal atom, alkaline earth metal atom, organic amine residue, basic amino acid residue or ammonium residue.

5 11. The penicillin derivative as defined in claim 1 wherein  $R_1$  and  $R_2$  are hydrogen.

*4D* 12. The penicillin derivative as defined in claim 1 wherein  $R_1$  is hydrogen and  $R_2$  is  $\bar{M}COOR_2'$ .

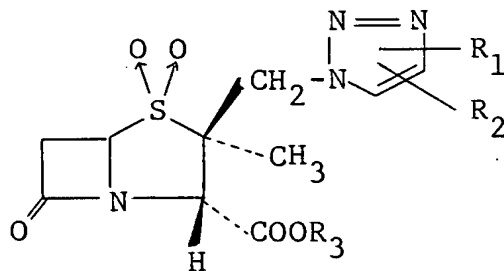
*4D* 10 13. The penicillin derivative as defined in claim 12 wherein  $R_2'$  is  $C_{1-18}$  alkyl.

*NK*  
*NP* 14. The penicillin derivative as defined in claim 11 or 12 wherein  $R_3$  is  $C_{3-8}$  alkylcarbonyloxymethyl, hydrogen,  $C_{4-9}$  alkylcarbonyloxyethyl, ( $C_{5-7}$  cycloalkyl)-carbonyloxymethyl,  $C_{9-14}$  benzylcarbonyloxyalkyl,  $C_{3-8}$  alkoxy carbonylmethyl,  $C_{4-9}$  alkoxy carbonylethyl, phthalidyl, crotonolacton-4-yl,  $\gamma$ -butyrolacton-4-yl, (5-substituted  $C_{1-6}$  alkyl or phenyl or unsubstituted-2-oxo-1,3-dioxolen-4-yl)methyl,  $C_{8-13}$  benzyloxyalkyl or group for forming a pharmaceutically acceptable salt.

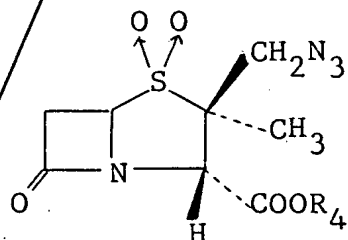
20 *14* 15. The penicillin derivative as defined in claim 1 wherein  $R_2$  is trialkylsilyl.

*NK*  
*NP* 16. A process for preparing a penicillin derivative represented by the following formula

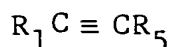
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wherein  $R_1$  is hydrogen or trialkylsilyl;  $R_2$  is hydrogen, trialkylsilyl or  $\text{COOR}_2'$  wherein  $R_2'$  is hydrogen,  $\text{C}_{1-18}$  alkyl,  $\text{C}_{2-7}$  alkoxyethyl,  $\text{C}_{3-8}$  alkylcarbonyloxyethyl,  $\text{C}_{4-9}$  alkylcarbonyloxyethyl, ( $\text{C}_{5-7}$  cycloalkyl)carbonyloxyethyl,  $\text{C}_{9-14}$  benzylcarbonyloxyalkyl,  $\text{C}_{3-8}$  alkoxy-carbonylmethyl,  $\text{C}_{4-9}$  alkoxy-carbonylethyl, phthalidyl, crotonolacton-4-yl,  $\gamma$ -butyrolacton-4-yl, halogenated  $\text{C}_{1-6}$  alkyl substituted with 1 to 3 halogen atoms,  $\text{C}_{1-6}$  alkoxy- or nitro-substituted or unsubstituted benzyl, benzhydryl, tetrahydropyranyl, dimethylaminoethyl, dimethylchlorosilyl, trichlorosilyl, (5-substituted  $\text{C}_{1-6}$  alkyl or phenyl or unsubstituted-2-oxo-1,3-dioxoden-4-yl)methyl,  $\text{C}_{8-13}$  benzoyloxyalkyl or group for forming a pharmaceutically acceptable salt; and  $R_3$  has the same meaning as above  $R_2'$ , the process comprising reacting a compound represented by the formula



wherein  $R_4$  represents penicillin carboxyl-protecting group with an acetylene compound represented by the formula

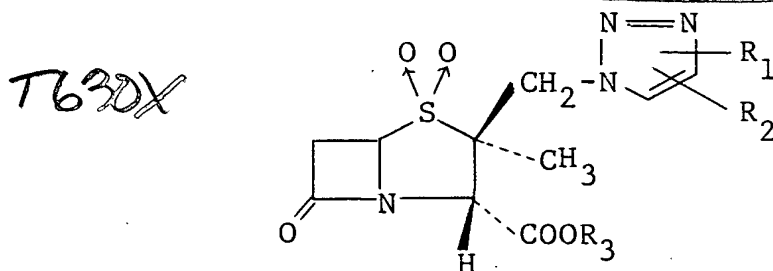


wherein  $R_1$  is as defined above and  $R_5$  is trialkylsilyl or  $COOR_2'$  wherein  $R_2'$  is as defined above and, when required, carrying out any of de-esterification, esterification subsequent to de-esterification, ester interchange reaction and salt-forming reaction.

10

15 A pharmaceutical composition useful for treating bacterial infections in mammals, *said composition comprising* which comprises

(A) a  $\beta$ -lactam antibiotic and (B) a compound of the formula



15

wherein  $R_1$  is hydrogen or trialkylsilyl;  $R_2$  is hydrogen, trialkylsilyl or  $COOR_2'$  wherein  $R_2'$  is hydrogen,  $C_{1-18}$  alkyl,  $C_{2-7}$  alkoxyethyl,  $C_{3-8}$  alkylcarbonyloxyethyl,  $C_{4-9}$  alkylcarbonyloxyethyl,  $(C_{5-7}$  cycloalkyl)carbonyloxyethyl,  $C_{9-14}$  benzylcarbonyloxyalkyl,  $C_{3-8}$  alkoxy-carbonylmethyl,  $C_{4-9}$  alkoxy-carbonylethyl, phthalidyl, crotonolacton-4-yl,  $\gamma$ -butyrolacton-4-yl, halogenated

20

C<sub>1-6</sub> alkyl substituted with 1 to 3 halogen atoms, C<sub>1-6</sub> alkoxy- or nitro-substituted or unsubstituted benzyl, benzhydryl, tetrahydropyranyl, dimethylaminoethyl, dimethylchlorosilyl, trichlorosilyl, (5-substituted

5 C<sub>1-6</sub> alkyl or phenyl or unsubstituted-2-oxo-1,3-dioxoden-4-yl)methyl, C<sub>8-13</sub> benzoyloxyalkyl or group for forming a pharmaceutically acceptable salt; and R<sub>3</sub> has the same

40 meaning as above R<sub>2</sub>', the weight ratio of (A)/(B) being

60 0.1 to 10, said  $\beta$ -lactam antibiotics being selected from

10 the group consisting of ~~penicillins such as~~ ampicillin, amoxicillin, hetacillin, ciclacillin, mecillinam, carbenicillin, sulbenicillin, ticarcillin, piperacillin, apalcillin, methicillin, mezlocillin, bacampicillin, carindacillin, talampicillin, carfecillin and

15 pivmecillinam; ~~cephalosporins such as~~ cephaloridine, cephalothin, cephapirin, cephacetrile, cefazolin, cephalixin, cefradine, cefotiam, cefamandole, cefuroxime, cefoxitin, cefmetazole, cefsulodin, cefoperazone, cefotaxime, ceftizoxime, cefmenoxime, latamoxef, cefaclor,

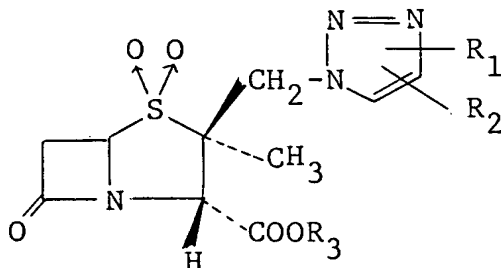
20 cefroxadine, cefatrizine, cefadroxil and cephaloglycin; and pharmaceutically acceptable salts thereof.

168. A method of treating a bacterial infection in a mammal <sup>said method comprising</sup> ~~subject which comprises administering~~ to said

60 subject (A) a  $\beta$ -lactam antibiotic and (B) a compound of

25 the formula

7650x



- wherein  $R_1$  is hydrogen or trialkylsilyl;  $R_2$  is hydrogen, trialkylsilyl or  $\text{COOR}_2'$  wherein  $R_2'$  is hydrogen,  $\text{C}_{1-18}$  alkyl,  $\text{C}_{2-7}$  alkoxymethyl,  $\text{C}_{3-8}$  alkylcarbonyloxymethyl,  $\text{C}_{4-9}$  alkylcarbonyloxyethyl, ( $\text{C}_{5-7}$  cycloalkyl)carbonyloxymethyl,  $\text{C}_{9-14}$  benzylcarbonyloxyalkyl,  $\text{C}_{3-8}$  alkoxy-carbonylmethyl,  $\text{C}_{4-9}$  alkoxy-carbonylethyl, phthalidyl, crotonolacton-4-yl,  $\gamma$ -butyrolacton-4-yl, halogenated  $\text{C}_{1-6}$  alkyl substituted with 1 to 3 halogen atoms,  $\text{C}_{1-6}$  alkoxy- or nitro-substituted or unsubstituted benzyl, benzhydryl, tetrahydropyranyl, dimethylaminoethyl, dimethylchlorosilyl, trichlorosilyl, (5-substituted  $\text{C}_{1-6}$  alkyl or phenyl or unsubstituted-2-oxo-1,3-dioxodene-4-yl)methyl,  $\text{C}_{8-13}$  benzoyloxyalkyl or group for forming a pharmaceutically acceptable salt; and  $R_3$  has the same meaning as above  $R_2'$ , the weight ratio of (A)/(B) administered being 0.1 to 10, said  $\beta$ -lactam antibiotics being selected from the group consisting of ~~penicillins~~ such as ampicillin, amoxicillin, hetacillin, ciclacillin, mecillinam, carbenicillin, sulbenicillin, ticarcillin, piperacillin, apalcillin, methicillin, mezlocillin,

65

*B*  
bacampicillin, carindacillin, talampicillin, carfecillin  
and pivmecillinam; ~~cephalosporins such as~~, cephaloridine,  
cephalothin, cephapirin, cephacetrile, cefazolin,  
cephalexin, cefradine, cefotiam, cefamandole, cefuroxime,  
5 cefoxitin, cefmetazole, cefsulodin, cefoperazone,  
cefotaxime, ceftizoxime, cefmenoxime, latamoxef, cefaclor,  
cefroxadine, cefatrizine, cefadroxil and cephaloglycin;  
and pharmaceutically acceptable salts thereof.

*66*